Remarks

Applicant respectfully requests reconsideration of this application in view of the amendments and remarks made herein. Claims 1-37 are currently pending.

Claims 1-37 are canceled, without prejudice. Applicants reserve the right to prosecute the subject matter of any canceled claims in one or more continuation, continuation-in-part, or divisional applications. Claims 1-37 have been replaced with new claims 38-53 which particularly point out and distinctly claim the subject matter that applicants regard as the invention, as discussed in detail herein. The new claims are fully supported by the specification and claims as originally filed, and, as such, no new matter has been added. Applicants respectfully request that the amendments and remarks made herein be entered into the record of the instant application.

1. Election/Restrictions

The Examiner alleges that newly submitted claims 28-37 are directed to an invention that is independent or distinct from the invention originally elected. According to the Examiner, the originally elected invention is directed to the use of a chimeric gene comprising a promoter which is induced at, and or adjacent to, a target site, wherein expression of the chimeric gene causes plant cytotoxicity at a target site, whereas the newly submitted claims are directed to the use of a chimeric gene comprising a tissue specific inducible promoter wherein the chimeric gene is expressed in and/or adjacent to a target tissue after induction, including uses wherein expression of the chimeric gene inactivates ribosomes in and/or adjacent to the target tissue of a solanaceous plant, and further including uses wherein expression of the chimeric gene confers nematode resistance or pollen sterility in a solanaceous plant. The Examiner has indicated withdrawal of claims 28-37 from consideration as being directed to a non-elected invention.

Applicants have canceled claims 28-37, without prejudice.

2. Claim Rejections Under 35 U.S.C. § 112, First Paragraph

A. The Invention Is Adequately Described in the Specification

Claims 7 and 10-13 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. According to the Examiner, Applicants have only described a single sequence that codes for a maize type 3 ribosome

inactivating protein (SEQ ID NO:2) and its parts (the *a* domain and the β domain, separated by a central peptide spacer and flanked by N and C terminal peptides) and not other sequences that code for a maize type 3 ribosome inactivating protein, or their parts. The Examiner maintains that since Applicants have not described a representative number of sequences that are homologous to SEQ ID NO:2 and that encode polypeptides that retain the activity of a maize type 3 ribosome inactivating protein, the genus of sequences recited in the claims is not described.

These rejections are inapposite and should be withdrawn because the specification does indeed describe the structural features of the nucleic acid molecules encompassed by the claims and demonstrates by way of examples the use of such DNA molecules.

Factors to be considered in determining whether there is sufficient written description include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function and method of making the claimed invention. Where the specification discloses relevant identifying characteristics, *i.e.*, physical, chemical and/or functional characteristics, sufficient to allow a skilled artisan to recognize that the applicant was in possession of the claimed invention, a rejection for lack of written description under Section 112, first paragraph, cannot be maintained. *Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 323 F.3d 956 (Fed. Cir. 2002).

The currently pending claims are directed to "a method of producing a transgenic solanaceous plant, wherein cells of the solanaceous plant have within their genome a chimeric gene, the expression of which gene causes plant cytotoxicity at a desired target site within the body of the plant, comprising transforming plant cells with a chimeric gene comprising (i) a promoter, which promoter is induced at and/or adjacent to a target site, operably linked to (ii) ***a nucleic acid molecule which encodes a protein having type 3 ribosome inactivating activity***."

Applicants maintain that support for the claimed invention can be found on p. 9, line 19, through p. 11, line 5, of the specification which discloses SEQ ID NO.: 2 and the stringent hybridization conditions that may be used to isolate additional sequences encoding a protein having ribosome inactivating activity. Furthermore, the working examples of the specification describe the actual isolation of a nucleic acid encoding a maize ribosome inactivating protein as

well as the use of assays for confirmation that the isolated nucleic acid molecule encodes a protein with ribosome inactivating activity.

Applicants submit that, given the teachings of the specification of both structural and functional features of the ribosome inactivating proteins encompassed by the claims, a sufficient written description has been provided. Therefore, the rejection is erroneous and applicants respectfully request withdrawal of these rejections under 35 U.S.C. § 112, first paragraph.

Applicants respectfully submit that the presently pending claims satisfy the written description requirement of 35 U.S.C. § 112, first paragraph.

B. Claims Are Enabled to Person of Skill in the Art to Practice Invention

Claims 1, 3, 7, 10-17, 21-23 and 26 remain rejected under 35 U.S.C. § 112, first paragraph. The Examiner maintains that the specification does not reasonably provide enablement for a method of producing a transgenic Solanaceous plant transformed with a chimeric gene comprising a coding sequence having 70-90% homology to SEQ ID NO:2 or encoding any unspecified part of a maize type 3 ribosome inactivating protein, the expression of which causes any unidentified type of plant cytotoxicity. Further, the Examiner asserts that the specification does not enable methods of producing transgenic plants transformed with chimeric genes further comprising transcriptional or translational enhancer sequences and/or intracellular targeting sequences and introns, and/or nucleotide sequences operable to facilitate the transformation process and stable expression of the chimeric gene because the specification fails to provide guidance with respect to which specific additional sequences to use or in what combination.

The test for enablement is whether one reasonably skilled in the art could make or use the invention, without undue experimentation, from the disclosure in the patent coupled with information known in the art at the time the patent application was filed. *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988).

As indicated above, the currently pending claims are directed to "a method of producing a transgenic solanaceous plant, wherein cells of the solanaceous plant have within their genome a chimeric gene, the expression of which gene causes plant cytotoxicity at a desired target site within the body of the plant, comprising transforming plant cells with a chimeric gene comprising (i) a promoter, which promoter is induced at and/or adjacent to a target site, operably

linked to (ii) a nucleic acid molecule which *encodes a protein having type 3 ribosome inactivating activity*."

Applicants maintain that, as indicated above, support for the claimed invention can be found on p. 9, line 19, through p. 11, line 5, of the specification which discloses SEQ ID NO.: 2 and the stringent hybridization conditions that may be used to isolate additional sequences encoding a protein having ribosome inactivating activity. Furthermore, the working examples of the specification describe the actual isolation of a nucleic acid molecule encoding a maize ribosome inactivating protein as well as the use of assays for confirmation that the isolated nucleic acid molecule encodes a protein with ribosome inactivating activity.

Applicants maintain that given that the specification discloses SEQ ID NO.: 2 and the stringent hybridization conditions, *including working examples which describe assays for detecting ribosome inactivating activity*, coupled with the knowledge of the skilled artisan at the time the invention was filed, undue experimentation would not have been required by one of skill in the art to develop and evaluate methods for generating the transgenic solanaceous plants encompassed by the claims.

With regard to the Examiner's comments concerning transgenic plants transformed with chimeric genes further comprising transcriptional or translational enhancer sequences and/or intracellular targeting sequences and introns, and/or nucleotide sequences operable to facilitate the transformation process and stable expression of the chimeric gene, the examiner is reminded that a patent need not teach, and preferably omits, what is well known in the art. *In re Buchner*, 929 F.2d 660 (Fed. Cir. 1991). Applicants assert that since transcriptional and translational enhancer sequences, intracellular targeting sequences, intron sequences, nucleotide sequences that facilitate the transformation process and stable expression of the chimeric gene are all well known to those of skill in the art, undue experimentation would not have been required by one of skill in the art to develop chimeric genes containing such elements.

Thus, given that the specification provides ample guidance to those skill in the art with regard to each of the issues raised by the Examiner, applicants respectfully request withdrawal of these rejections of claims under 35 U.S.C. § 112, first paragraph.

3. Claim Rejections Under 35 U.S.C. § 112, First Paragraph

The Examiner has rejected claims 1, 21-23, and 26 under 35 U.S.C. § 112, second paragraph, as being indefinite in the recitation of "target site" and "which promoter is induced at and/or adjacent to a target site."

Applicants have amended the claims to indicate that the expression of the chimeric gene causes "plant cytotoxicity at a desired target site within the plant body." The claims as amended indicate that the target site is a location within the plant body where expression of the chimeric gene occurs and selective cytotoxicity is desired.

In view of the amendments to the claims, the rejections under 35 U.S.C. § 112, second paragraph, should be withdrawn.

4. Claim Rejections Under 35 U.S.C. § 101

Claim 22 is rejected under 35 § U.S.C. 101. The Examiner alleges that the claimed invention is directed to non-statutory subject matter as the claim does not require that the claimed cell itself comprise the chimeric gene.

Applicants have canceled claim 22 and replaced it with new claim 50. New claim 50 specifies that the claimed plant cell comprises "within its genome a chimeric gene." In view of the amendment to the rejected claim, the rejection under 35 U.S.C. § 101, should be withdrawn.

5. The Claims Are Not Anticipated by Maddaloni *et al.*

Claims 1, 7, 10-17, 21-23, and 26 are rejected under 35 U.S.C. § 102(b) as being anticipated by Maddaloni *et al.* (Transgenic Research, 1997 6:393-402: "Maddaloni"). According to the Examiner, Maddaloni *et al.* teach a method of producing a transgenic tobacco plant transformed with a chimeric gene comprising a potato wound-inducible *wun 1* promoter operably linked to a coding sequence encoding a maize ribosome inactivating protein.

Maddaloni does not anticipate the presently claimed invention. Maddaloni fails to describe the selective expression of a ribosome inactivating protein to a specific location within the plant body, *i.e*, a target site, ***for induction of plant cell death*** at that location."An anticipatory reference must sufficiently describe and enable the claimed invention in such a way as to have placed the public in possession of it." *Paperless Accounting, Inc. v. Bay Area Rapid Transit System*, 804 F.2d 659 (Fed. Cir. 1986). Further, in order for a reference to anticipate a

claim, each and every element of the claim must be disclosed in that one reference. *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565 (Fed. Cir. 1985). "Anticipation under Section 102 can be found only if a reference shows exactly what is claimed. . ." *Structural Rubber Prod. Co. v. Park Rubber Co.*, 749 F.2d 707 (Fed. Cir. 1984).

Ribosome inactivating proteins are known to be potent inhibitors of protein translation. The present invention is directed to the use of ribosome inactivating proteins in a plant cell death system wherein selective gene expression of ribosome inactivating proteins to a targeted location within a transgenic plant, *i.e.*, a target site, leads to plant cell death at that location. Selective gene expression is facilitated through the use of a chimeric gene containing a promoter which is active at the desired target site. As disclosed in the specification, such selective expression of ribosome inactivating proteins, may have multiple uses, including destruction of nematode feeding sites, induction of plant sterility, changes to flower morphology, and promotion of leaf or fruit abscission, to name a few.

Applicants assert that although Maddaloni discloses the expression of a maize ribosome-inactivating protein, in tobacco, under the control of the potato wun1 gene promoter, Maddaloni's tobacco plants were not designed to target plant cell death, but rather to target fungal cell death. That the disclosure of Maddaloni is directed to methods for inducing fungal cell death, and not plant cell death, is demonstrated by Maddaloni's statement "that a major factor limiting the potential activity of ribosome inactivating proteins as plant defensive molecules is related to the ability of such proteins to enter ***the fungal cell wall***." (See, p. 400, column 2, lines 2-5).

In fact, Maddaloni teaches away from the invention in his discussion of the ***problem of cytotoxicity of RIPs on host cells***. (*See*, p.400, column 1, first full paragraph). For example, Maddaloni acknowledges the susceptibility of plant ribosomes to the action of ribosome inactivating proteins, as well as the ability of pokeweed ribosome inactivating proteins to cause severe plant deformities. Thus, Maddaloni states that "..it might be speculated that the use of high catalytic activity RIPS might not necessarily be the most appropriate strategy to be adopted in plant protection." (See, Maddaloni, p. 400, first full paragraph, lines 13-17). The Examiner is reminded that a prior art reference must be considered in its entirety, *i.e.*, as a whole, including portions that would lead away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540 (Fed Cir. 1983, cert denied, 469 U.S. 851 (1984).

Moreover, Maddaloni even presents possible solutions for preventing cytotoxicity, which is the opposite goal of the present invention, while retaining the ability to protect plants from pathogens. Such solutions include, for example, "using a RIP with a proper level of activity and a suitable promoter or on the utilization of efficient systems for quick export of the protein from the cytoplasm." (*See*, Maddaloni, p. 400, column 1, line 23, through column 2, line 2). Such quick export would be designed to prevent inactivation of plant cell ribosomes.

Given that Maddaloni fails to disclose the use of target tissue selective localized expression of a ribosome inactivating protein for induction of plant cell death, as required by the currently pending claims, the claimed invention simply cannot be anticipated by Maddaloni. Accordingly, Applicants request withdrawal of the rejection of the claims as anticipated by Maddaloni.

5. The Claims Are Not Obvious Over Cited Art

Claims 1, 3, and 14-17 remain rejected under 35 U.S.C. 103(a) as being unpatentable as obvious over Maddaloni in view of Hey *et al.* (Plant Physiology, 1995, 107:1323-1332:"Hey")and Boston *et al.* (US Patent No. 5,332,808: "Boston"). According to the Examiner, the rejected claims encompass producing a transgenic plant by using a chimeric gene comprising any unspecified promoter which is induced at and/or adjacent to any unspecified target site, wherein expression of the gene causes plant cytotoxicity at a target site. The Examiner maintains that the rejected claims encompass the use of the potato wound-inducible wun1 promoter as taught by Maddaloni, which is induced by wounding at, and or adjacent to, a wounding target site.

According to the Examiner, although Maddaloni does not teach the use of a recombinant mature maize ribosome inactivating protein comprising an α domain and a β domain arranged contiguously, or the use of nos terminator in a plant, Hey teaches a biologically active recombinant mature maize ribosome inactivating protein comprising an α domain and a β domain arranged contiguously, and Boston teaches the use of a nos terminator in a plant expression construct design to express a sequence encoding a maize ribosome activating protein. Thus, according to the Examiner, the claimed invention would have been *prima facie* obvious as a whole to one of ordinary skill in the art at the time the invention was made.

A finding of obviousness under 35 U.S.C. § 103 requires a determination of: (1) the

scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the difference between the claimed subject mater and the prior art; and (4) whether the differences are such that the subject matter as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made. *Graham v. Deere* 383 U.S. 1 (1966). The prior art relied upon by an examiner to establish a prima facie case must not only suggest that the claimed method be performed, but the prior art must also provide one of ordinary skill in the art with a reasonable expectation that the claimed subject matter can be successfully used to effect a practical purpose. *In re Vaeck*, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991.

As discussed above, Maddaloni simply fails to disclose, or even suggest, the use of a inducible promoter to achieve specific localized expression of maize type 3 ribosome inactivating protein at and/or adjacent to a target site in a host plant to ***induce plant cell death*** at that target site. Rather, Maddaloni teaches increased tolerance against infection from a soil-borne fungal pathogen by directing ribosome inactivating protein activity toward the invading pathogen, *i.e.*, to ***induce fungal cell death***.

In fact, as indicated above, Maddaloni actually teaches away from the invention in his discussion of the ***problem of cytotoxicity of RIPs on host cells.*** (*See*, Maddaloni, p.400, column 1). It is noteworthy that with regard to this particular section of Maddaloni, the Examiner concludes that "the induction of localized plant cell death could be considered a desirable phenotypic trait in response to certain plant pathogens." (*See*, p.11, line 19 through p.12 line 16, of the Office Action). However, there is absolutely no such disclosure, or suggestion, to be found in Maddaloni to support the Examiner's statement that such plant cell death is desirable. Indeed, Maddaloni suggests methods for avoiding plant cell death. (*See*, Maddaloni, p.400, column 1, line 19, through column 2, line 2).

With regard to the Hey and Boston references, Applicants assert that neither reference makes up for the deficiencies of Maddaloni. Neither reference discloses, teaches, or suggests the use of target tissue selective localized expression of a ribosome inactivating protein for induction of plant cell death.

Since none of the cited references, alone or in combination, disclose, teach, or suggest the subject matter of the pending claims, Applicants respectfully request that the Examiner withdraw the rejection of these claims as obvious over Maddaloni in view of Hey and Boston.

CONCLUSION

Applicants respectfully submit that all pending claims 38-53 are presently in condition for allowance. Prompt and favorable reconsideration and allowance of all pending claims is respectfully requested.

The Commissioner is authorized to charge any fees relevant to this filing to Deposit Account No. 11-0600. The Examiner is invited to contact the undersigned to discuss any matter in this application.

Respectfully submitted,

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